

**AMENDMENTS TO THE CLAIMS:**

The following listing of claims will replace all prior versions and listings of claims in the application:

*Pending*  
*50-54, 68-79*

1-49. (Cancelled)

~~50.~~ (Previously presented) A method of producing a human neural progenitor cell from a human ES cell, said method comprising:

obtaining a source of an undifferentiated human ES cell; and  
culturing the ES cell in the presence of an antagonist of a BMP mediated default pathway of extra embryonic endoderm differentiation to differentiate the ES cell to a progenitor cell, wherein said progenitor cell lacks at least one marker of said undifferentiated ES cell; and  
culturing the progenitor cell in a neural progenitor cell culture medium to obtain a neural progenitor cell.

~~51.~~ (Previously presented) The method of claim 50 wherein the source of said undifferentiated human ES cell is selected from the group consisting of an embryo, a blastocyst, and a culture of undifferentiated embryonic stem cells.

~~52.~~ (Previously presented) The method of claim 51 wherein said antagonist is noggin.

~~53.~~ (Previously presented) The method of claim 52 wherein said noggin is a human or mouse noggin.

~~54.~~ (Previously presented) The method of claim 52 wherein said noggin is a mouse BMP antagonist noggin comprising amino acid residues 20 to 232 of mouse noggin.

~~55.~~ (Previously presented) The method of claim 52 wherein said noggin is in the range of 100 to 500 ng/ml.

~~56.~~ (Previously presented) The method of any one of claims 50 to 55 wherein the ES cell is differentiated to a said progenitor cell is by culturing the ES cell in the presence of noggin for at least 5 days, wherein the noggin is in the range of 100 to 500 ng/ml.

57-67. (Cancelled)

~~68.~~ (Previously presented) The method of claim 50 wherein said at least one marker of said undifferentiated ES cell is Oct-4 or cripto.

~~69.~~ (Previously presented) A method of producing a human progenitor cell from a human ES cell, said method comprising:

- obtaining a source of an undifferentiated human ES cell; and
- culturing the ES cell in the presence of an antagonist of a BMP mediated default pathway of extra embryonic endoderm differentiation under conditions sufficient to differentiate the ES cell to a progenitor cell, wherein said progenitor cell lacks at least one marker of said undifferentiated ES cell, lacks a marker of neuroectoderm, and is capable of differentiating into a neural progenitor cell.

~~70.~~ (Previously presented) The method of claim 69 wherein said antagonist is noggin.

~~71.~~ (Previously presented) The method of claim 70, wherein the ES cell is cultured in the presence of noggin for at least 5 days.

~~72.~~ (Previously presented) The method of claim 70 wherein said noggin is a human or mouse noggin.

~~73.~~ (Previously presented) The method of claim 72 wherein said noggin is comprises amino acid residues 20 to 232 of mouse noggin.

~~74.~~ (Previously presented) The method of claim 70 wherein said noggin is in the range of 100

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to 500 ng/ml.

~~75.~~ (Previously presented) The method of claim 69 wherein the source of said undifferentiated human ES cell is selected from the group consisting of an embryo, a blastocyst, and a culture of undifferentiated embryonic stem cells.

~~76.~~ (Previously presented) The method of claim 69, wherein said at least one marker of said undifferentiated ES cell is Oct-4 or cripto.

~~77.~~ (Previously presented) The method of claim 69, wherein said marker of neuroectoderm is nestin or Pax 6.

~~78.~~ (Previously presented) The method of claim 69, wherein said progenitor cell is unreactive with any one of the antibodies selected from the group consisting of PHM4 recognising MHC Class 1 surface molecules, anti-desmin, UJ13A reactive with polysialylated N-CAM, Cam 5.2 reactive with low molecular weight cytokeratins, AMF reactive with vimentin intermediate filaments, antibody to 160 kDa neurofilament protein, GCTM-2 reactive with a proteoglycan present on the surface of ES cells, TG42.1 reactive with a 25 kDa protein which copurifies with the proteoglycan recognised by GCTM-2 and is found on stem cells and other cell types, and monoclonal antibody GCTM-5 reactive with a molecule present on a small proportion of cells in spontaneously differentiating human ES cell cultures.

~~79.~~ (Previously presented) The method of claim 69, wherein said progenitor cell, upon further culturing in a neural progenitor culture medium, differentiates into said neural progenitor cell.

80-83. (Canceled)

**CLAIMS**

1. A method for modulating spontaneous differentiation of a stem cell, which method comprises incubating the stem cell in the presence of an agonist of a LPL receptor.  
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2. A method for modulating spontaneous differentiation of a stem cell, which method comprises incubating the stem cell in the presence of a ligand of a class III tyrosine kinase receptor.
3. A method for modulating spontaneous differentiation of a stem cell, which method comprises incubating the stem cell in the presence of an agonist of a LPL receptor and a ligand of a class III tyrosine kinase receptor.  
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4. A method according to claim 1 wherein the modulation is inhibition of differentiation.
5. A method according to claim 1 wherein the LPL receptor is selected from the group consisting of S1P1, S1P2, S1P3.  
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6. A method according to claim 1 wherein the agonist is a phospholipid.
7. A method according to claim 6 wherein the agonist is selected from the group consisting of S1P, dihydro S1P, LPA, PAF and SPC or functional equivalents thereof.
8. A method according to claim 7 wherein the agonist is S1P or functional equivalent thereof.  
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9. A method according to claim 7 wherein the agonist is dihydro S1P or functional equivalent thereof.
10. A method according to claim 2 wherein the tyrosine kinase receptor is PDGFR- $\alpha$  or PDGFR- $\beta$ .  
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11. A method according to claim 2 wherein the ligand is a PDGF or functional equivalent thereof.
12. A method according to claim 11 wherein the PDGF is PDGF $\alpha\alpha$ , PDGF $\alpha\beta$  or PDGF $\beta\beta$ .
13. A method according to claim 1 comprising use of TNF alpha, NGF (nerve growth factor), a muscarinic acetylcholine agonist, or a serum or phorbol ester.  
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